BRIDGE

Bridging knowledge in GI cancers

BRIDGE is an initiative by SERVIER that connects health care professionals worldwide, to share knowledge and unite actions for the benefit of GI cancer patients.

Treatment strategy in mPaCa: extending the continuum of care?

Webinar No 12
HIGHLIGHTS

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Prof Prager is the Director of the GI Cancer Program in the Department of Medical Oncology at the Medical University of Vienna and Comprehensive Cancer Center, Vienna. He leads the unit for Precision Medicine in Cancer and is an associate professor of medicine, board certified for internal medicine, hematology, and medical oncology. Prof Prager graduated from the Medical School of the University of Vienna and completed his postdoctoral training at the University of California, San Diego, USA and was a visiting professor at the Norris Cancer Center, University of Southern California, Los Angeles, USA in 2011. Prof Prager's main research interests focus on translational research and (tumor-) angiogenesis, and his works have been honored by more than 20 international awards and published in highly renowned international journals. Prof Prager is also a member of the ESMO Scientific Committee.

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WEBINAR HIGHLIGHTS

Pancreatic cancer is a disease with a poor prognosis and is set to become the **second cause of death from cancer** worldwide.[1]

Incidence and **mortality** rates are estimated to **increase by 61.7% and 64.2%,** respectively, by 2040.[2]

Asia and **Europe** had the highest incidence and mortality rates in 2020.[1]

The objectives of treatment are **maintenance of quality of life** and **improvement of prognosis.** Defining **treatment planning from the start** will help to **optimize and extend the continuum of care** for patients with mPaCa.*

INTERACTIVE CLINICAL CASE†

Our patient:

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Patient profile	Male, 67 y/o, retired but still active, BMI 29 ECOG PS 0
Medical history	No prior surgical resection, art. hypertension, controlled diabetes
Symptoms	≈5% weight loss, abdominal pain, and back pain (controlled by painkillers)
Bloodwork	CA19-9: 2650 kU/l; bilirubin: 1.1 mg/dL
Tests performed	CT scan, biopsy of peritoneum metastasis
Tumor sites	Primary: pancreatic head; metastasis: peritoneum
Molecular profile	KRAS G12D mt, MSS, BRCA wt
Diagnosis	Metastatic pancreatic cancer

Results from polls‡

What would you give in 1L?

Gemcitabine + nab-paclitaxel	47%
FOLFIRINOX	42%
Gemcitabine + cisplatin	9%
Gemcitabine monotherapy	2%

What's the main factor behind this treatment decision?

Phase 3 efficacy	40%
Treatment planning strategy	28%
Patient characteristics	26%
Safety profile	6%

1L treatment choice

Speaker's recommendations: gemcitabine + nab-paclitaxel
Why? Treatment planning strategy

IMPACT OF TREATMENT PLANNING†

Change in treatment patterns in the past decade:

- An increase of **frontline use of gem + nab-P** (**69%** in 2014-2017 **vs 26%** in 2011-2013) has led to a **higher usage of nal-IRI as 2L treatment**[3]
- More patients **have started 3L therapy** (**37%** in 2014-2017 **vs 26%** in 2011-2013)[3]
- Furthermore, in 1L treatment choice, **gem + nab-P** appears to have a **better safety profile** than FOLFIRINOX but seems to have a comparable efficacy[4,5]

Increase in overall survival:

- Extending overall survival **in 1L** (**11.9 mo** in 2014-2017 **vs 8.89 mo** in 2011-2013)[3]
- Improved overall survival **in 2L** (**9.39 mo** in 2014-2017 **vs 7.14 mo** in 2011-2013)[3]

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Patient follow-up in 1L treatment:

April

Initial treatment:
Gemcitabine 1000 mg/m² + nab-P 125 mg/m²
Days 1, 8 and 15 of 28-day cycle

CT scan at diagnosis (pancreatic head cancer with multiple peritoneal metastases)

June

After cycle 2:
Abdominal, back pain disappeared
Toxicity: fatigue grade 1, neuropathy grade 2

CT scan at 2 months: PR
CA19-9 kU/l: 276

January

Progressive disease after cycle 9
ECOG PS: 1

CT scan at 9 months shows SD in pancreatic mass with new lesions in peritoneum CA19-9 kU/l: 1250

Results from polls‡

What would you give in 2L?

Nal-IRI + 5-FU/LV	80%
mFOLFOX	4.5%
(m)FOLFIRINOX	9%
Gemcitabine monotherapy	2%
OFF	4.5%

2L treatment choice

Speaker's recommendations:
Nal-IRI + 5-FU/LV

- **Nal-IRI + 5-FU/LV significantly improved overall survival (6.2 vs 4.2 mo** in NAPOLI-1 trial), **PFS, ORR and DCR** compared with other 2L treatment options.[6,7]
- Real-world data revealed that **nal-IRI + 5-FU/LV had better efficacy when administered in 2L** than when administered in later lines.[7]

Patient follow-up in 2L treatment:

February

Nal-IRI 70 mg/m² + 5-FU 2100 mg/m² + LV 400 mg/m²
Weight loss: 4 kg

CT scan at initiation of 2L
CA19-9 kU/l: 1415

April

During treatment: fatigue, grade 3 neutropenia, grade 1 diarrhea
Weight gain: 5 kg

CT scan at 2 months: PR
CA19-9 kU/l: 345

August

Progressive disease after 6 months
ECOG PS:1
Grade 1 diarrhea
Weight loss: 2 kg

CT scan at 6 months: PR
CA19-9 kU/l: 747

Management of side effects

Speaker's recommendations:

- **1L:** discuss fatigue; monitor blood cell count, albumin level and peripheral neuropathy, engage in physical therapy
- **2L:** proactively discuss the possibility of diarrhea and how to manage this, monitor blood cell count, and in case of weight loss, discuss nutrition.

Stop and adapt treatment before serious adverse events emerge!

IN CONCLUSION

- In fit patients with mPaCa, **gem + nab-P or mFOLFIRINOX** are the preferred 1L treatment options with similar efficacy but a **better safety profile for gem + nab-P**[4,5]
- Higher usage of **nal-IRI as a 2L treatment** option led to **more patients starting 3L therapy** and **increased median survival**[3]
- Both phase 3 trials and real-world evidence have shown nal-IRI + 5-FU/LV to be an effective 2L treatment option that is significantly **more effective than when given in later lines**[6,7]
- **Nal-IRI + 5-FU/LV is the only recommended (NCCN and ESMO) treatment** in patients who have progressed following gemcitabine-based therapy. It is therefore important to **factor 2L from the start, when choosing 1L treatment,** in order to **ensure the best treatment sequence as well as prognosis for your patient**
- Adverse events and disease-related symptoms should be addressed **proactively**

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for more details and watch the replay of the 13/01/2022 session

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INSIGHTS FROM THE EXPERT'S CLINICAL PRACTICE

"Pancreatic cancer is different to other solid tumors because we also have to treat the tumor microenvironment and not just the tumor cells."

"Nal-IRI + 5-FU/LV is meant for fit patients (ECOG PS 0-1). Patients should be educated about diarrhea. For early onset diarrhea, like with irinotecan, use atropine. For late onset diarrhea, when patients are back at home, have them use loperamide, which helps them pretty well."

"I test for BRCA germline mutations but only in the metastatic setting. In my experience, it really tends to vary on ethnicity and country, but BRCA germline mutations seem to be present in 3-5% of the patient population."

"Unlike other cancers, immunotherapy seems to have little to no impact in mPaCa. Patients with MSI-H tumors seem to benefit from immunotherapy but they are a rare type of patient."

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*Based on speaker's interpretation of clinical data
†Based on speaker's clinical experience
‡ These results are based on the average of the two live webinar sessions. They reflect the votes of the audience that attended the sessions and do not reflect Servier's view or the PIs. Please always refer to your relevant PIs and regulatory compliance. The audience was a total of 154 physicians from 26 countries.

1L: first line; 2L: second line; 3L: third line; 5-FU: 5-flourouracil; art.: arterial; BMI: body mass index; BRCA: breast cancer gene; CA19-9: carbohydrate antigen 19-9; CT: computerized tomography; DCR: disease control rate; ECOG PS: Eastern Cooperative Oncology Group performance status; ESMO: European Society of Medical Oncology; FOLFIRINOX: leucovorin + fluorouracil + irinotecan + oxaliplatin; gem: gemcitabine; GI: gastrointestinal; KRAS G12D mt: G12D mutation of KRAS gene; LV: leucovorin; mFOLFIRINOX: modified FOLFIRINOX regimen; mFOLFOX: modified leucovorin + fluorouracil + oxaliplatin regimen; mo: months; mPaCa: metastatic pancreatic cancer; MSI-H: high microsatellite instability; MSS: microsatellite stable; nab-P: nab-paclitaxel; nal-IRI: liposomal irinotecan; NCCN: National Comprehensive Cancer Network; OFF: oxaplatin + folic acid + fluorouracil; ORR: objective response rate; PFS: progression-free survival; PI: prescribing information; PR: partial response; SD: structural damage; wt: wild type; y/o: years old

References: 1. Globocan 2020 – Pancreas. Accessed Dec 2021. gco.iarc.fr/today/data/factsheets/cancers/13-Pancreas-fact-sheet.pdf. 2. Globocan 2020 – Cancer tomorrow. Accessed Dec 2021. gco.iarc.fr/tomorrow/en/dataviz/tables?cancers=13&single_unit=50000&age_end=17&mode=population&types=0. 3. Kieler M et al. Impact of New Chemotherapy Regimens on the Treatment Landscape and Survival of Locally Advanced and Metastatic Pancreatic Cancer Patients. J Clin Med. 2020;9;1-15. 4. Conroy T et al. FOLFIRINOX versus Gemcitabine for Metastatic Pancreatic Cancer. N Engl J Med. 2011;364:1817-1825. 5. Von Hoff DD et al. Increased Survival in Pancreatic Cancer with nab-Paclitaxel plus Gemcitabine. N Engl J Med. 2013;369:1691. 6. Wang Gillam A et al. NAPOLI-1 phase 3 study of liposomal irinotecan in metastatic pancreatic cancer: Final overall survival analysis and characteristics of long-term survivors. Eur J Cancer. 2019;108:78-87. 7. Kieler M et al. T A real-world analysis of second-line treatment options in pancreatic cancer: liposomal-irinotecan plus 5-fluorouracil and folinic acid. her Adv Med Oncol. 2019;11:1-13.

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Available on replay

Bridge season 1

Third-line therapy in mCRC live conference
Prof Julien Taieb

Continuum of care in mPaCa live conference
Prof Gerald Prager

Treating mPaCa patients: from scientific evidence to real clinical practice
Prof Teresa Macarulla

Addressing the unmet needs in 3L mGC: a clinical perspective
Prof Sylvie Lorenzen & Dr Elizabeth Smyth

mPaCa clinical cases: experience sharing from Asia and Europe
Prof Junji Furuse & Prof Ivan Vilmos Borbath

Maximizing benefit for patients in 3L mCRC, clinical case discussion
Prof Timothy Price

Management of mPaCa patients in Asia: what are the specific features compared with the rest of the world?
Prof Changhoon Yoo

Challenges in the management of GI cancer, a clinical perspective on 3L mCRC & mGC
Prof Florian Lordick & Prof Pia Österlund

Where do we stand in mPaCa?
Prof Thomas Seufferlein

Bridge season 2

New evidence on 3L mGC, applied to daily practice
Prof Sylvie Lorenzen & Prof Aziz Zaanan

Treatment strategy in mPaCa: extending the continuum of care
Prof Gerald Prager

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Upcoming webinar

Extending the continuum of care in 3L mCRC: from scientific evidence to daily clinical practice

Prof Chiara Cremolini
Associate Professor in Medical Oncology, University of Pisa, Italy

Tuesday, April 26, 2022
5:30 PM CET
CLICK HERE
to register

Dr Anelisa Coutinho
Clinical oncologist and coordinator of the Gastrointestinal Tumors department, Clínica AMO of Salvador, Brazil

Thursday, April 28, 2022
7 PM CET
CLICK HERE
to register

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